

Epidemiologic features of hepatitis B virus infection in northern Labrador

Maureen Baikie, MD
Samuel Ratnam, PhD
David G. Bryant, PhD
Michael Jong, MD
Maarten Bokhout, MD

We studied the epidemiologic features of hepatitis B virus (HBV) infection in northern Labrador to determine the prevalence of the infection and to obtain a database to develop a vaccination strategy. The study population included seven communities in which five ethnic groups were represented: Inuit, Innu, mixed Inuit and European ancestry ("settler"), nonnative/nonsettler transient population ("white") and people of Innu-white or Innu-Inuit origin ("mixed"). Blood samples from 2156 people (62% of the area residents) were tested for antibody to HBV core antigen (anti-HBc), HBV surface antigen (HBsAg), HBV e antigen (HBeAg), anti-HBc IgM and antibody to the surface antigen (anti-HBs). The overall crude prevalence rate of HBV seromarkers was 14.7% and the HBsAg carrier rate at least 3.2%; the rates were highest for Inuit (26.4% and 6.9% respectively), followed by settler (10.0% and 1.9% respectively) and Innu (7.6% and 0.4% respectively); the white and mixed groups had the lowest overall rates (2.5% and 3.3% respectively). Although the overall prevalence rates were about the same for the two sexes, the HBsAg carrier rate was higher in males (male:female ratio 1.6:1.0). No HBV carriers were positive for HBeAg or anti-HBc IgM antibody. The rate of exposure to HBV was 4% for those below the age of 20 years and reached a peak for those aged 45 to 54 years (85% for Inuit, 40% for settlers and 37% for Innu). There was also a

wide variation in the age-standardized prevalence rates (0% to 27.9%) among the ethnic groups in the seven communities surveyed.

Étude de l'épidémiologie de l'infection par le virus de l'hépatite B (HBV) dans le nord du Labrador, afin d'établir les bases d'un programme de vaccination. La population en cause habite sept agglomérations et représente cinq groupes ethniques: les Inuit, les Montagnais, les "colons" (d'ascendance mixte inouke-européenne), les "blancs" (résidents de passage ni aborigènes ni colons), les "mixtes" (d'ascendance montagnaise-blanche ou montagnaise-inouke). On prélève le sang de 2156 personnes, soit 62% de la population, et recherche l'anticorps contre l'antigène nucléocapsidique (anti-HBc), l'antigène HBV de surface (HBsAg), l'antigène HBV e (HBeAg), l'immunoglobuline M (IgM) anti-HBc et l'anticorps contre l'antigène de surface (anti-HBs). La fréquence globale de la présence de séromarqueurs chez ces personnes est de 14,7%, et le taux de porteurs de HBsAg est d'au moins 3,2%. Les taux respectifs sont plus élevés chez les Inuit (26,4% et 6,9%); viennent ensuite les colons (10,0% et 1,9%) et les Montagnais (7,6% et 0,4%). Les taux globaux les plus bas se trouvent chez les blancs (2,5%) et les mixtes (3,3%). La seule différence selon le sexe est dans le taux de porteurs de HBsAg, qui est plus haut chez les hommes que chez les femmes (rapport 1,6). Aucun porteur de HBV ne donne de résultat positif pour HBeAg ou pour l'IgM anti-HBc. Le taux d'un contact antérieur avec HBV, qui est de 4% avant 20 ans, atteint un pic entre 45 et 54 ans (85% chez les Inuit, 40% chez les colons et 37% chez les Montagnais). Les fréquences normalisées quant à l'âge varient beaucoup (de 0 à 27,9%) d'un groupe à l'autre dans les sept agglomérations.

From the Labrador Inuit Association, Nain, Nfld., the Newfoundland and Labrador Public Health Laboratory, St. John's, Memorial University of Newfoundland, St. John's, and Grenfell Regional Health Services, Goose Bay and St. Anthony, Nfld.

Presented in part at the 7th International Congress on Circumpolar Health, Umea, Sweden, June 8 to 12, 1987

Reprint requests to: Dr. Samuel Ratnam, Public Health Laboratory, PO Box 8800, St. John's, Nfld. A1B 3T2

The native populations in some communities of northern Canada, Alaska and Greenland have a significantly higher prevalence of hepatitis B virus (HBV) infection than nonnatives in southern Canada and the United States.¹⁻³ These findings have led to hepatitis B vaccination programs in some areas.⁴

A preliminary study in Labrador indicated a higher prevalence of HBV infection in the native population than in the nonnative population.⁵ Prompted by this observation, a serologic survey of seven northern Labrador communities was conducted jointly by the Labrador Inuit Association, Grenfell Regional Health Services and the Provincial Public Health Laboratory during the first half of 1986 to establish a database on HBV infection with a view to further defining the problem in relation to other circumpolar areas. In this paper we present the serosurvey data, which will be used to develop a vaccination strategy adjustable to the pattern of the disease in each community.

Labrador is situated on the northeastern tip of North America and forms part of the Canadian province of Newfoundland and Labrador. Five ethnic groups were represented in the seven communities: Inuit (Eskimo), Innu (indigenous Indians), people of mixed Inuit and European ancestry ("settler"), transients of nonnative origin who are mainly white ("white") and people of Innu-white or Innu-Inuit origin ("mixed") (Fig. 1). The seven communities could also be considered to represent three community groups: group I is predominantly Inuit (communities A and B), group II predominantly settler (communities C, D and E) and group III predominantly Innu (communities F and G). The 1986 Canadian census put the total population of these seven communities at 3470.

Many of the Inuit, Innu and settler pursue the traditional lifestyle of hunting, trapping and fishing. The unemployment rate is high. Housing is often poor and overcrowded. Water and sewer systems range from virtually nonexistent to adequate. There is frequent travel between communities. Each community has a Grenfell Regional Health Services nursing station staffed by nurse-practitioners and visiting physicians. Referrals are made to a hospital in central Labrador. The Labrador Inuit Health Commission operates a health education and promotion program through its community health representatives.

Methods

Consultation with various community groups was held, and a comprehensive public health information campaign regarding hepatitis B was launched. The entire population from each community was asked to participate in the serosurvey.

Blood samples were collected by venipuncture. All samples were screened for antibody to HBV core antigen (anti-HBc), and those yielding positive results were tested for anti-HBc IgM-

specific antibody, HBV surface antigen (HBsAg) and antibody to the surface antigen (anti-HBs). Samples positive for HBsAg were further tested for HBV e antigen (HBeAg). The samples negative for anti-HBc were not tested further. Throughout the survey enzyme immunoassays (Abbott Laboratories, North Chicago) were used to test for the various HBV seromarkers.

We compared the standardized prevalence rates of HBV seropositivity for each ethnic group in each community using Tukey's w-procedure at a 95% confidence level;⁶ this procedure allowed multiple comparisons without reduction in the level of confidence. The age-standardized prevalence rates were calculated by means of the direct method based on the pooled data for the sampled subjects.⁷ These standardized rates were calculated for each ethnic group in each community.

Results

A total of 2156 people (62% of the target population in the seven communities) participated in the survey. The participation rates for the communities and the ethnic groups are shown in Table I. The male to female ratio was 1.1:1. The age of the subjects ranged from 8 days to 88 years. Only one-third of those aged 4 years or younger participated in the survey, owing to the technical difficulty in obtaining blood from small children and the unwillingness of some parents to allow their infants to be tested. For the remaining age groups the participation rates ranged from one-half to three-quarters.

Evidence of HBV infection (i.e., anti-HBc) was found in 317 (14.7%) of the 2156 people tested (Table II). Of the 317 about two-thirds were also positive for anti-HBs, 69 for HBsAg and none for HBeAg or anti-HBc IgM. There was a marked

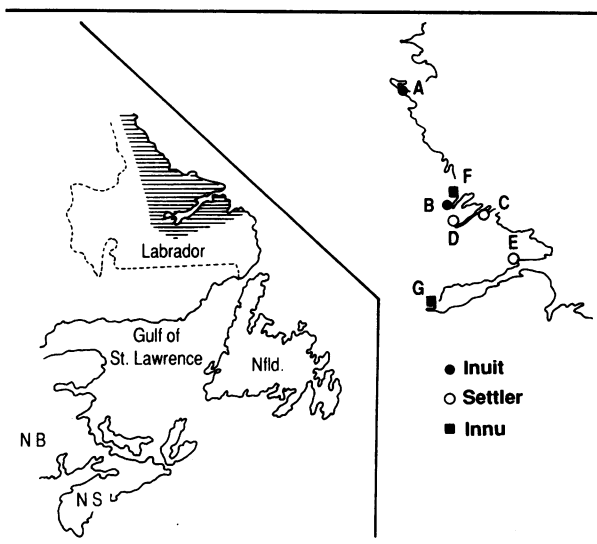


Fig. 1 — Location of communities and predominant ethnic groups in hepatitis B serosurvey in northern Labrador.

difference in the crude prevalence rates of HBV seromarkers among the five ethnic groups. We therefore examined the ratio of HBsAg-positive cases to those positive only for the antibodies in each ethnic group. The ratio was higher among the Inuit (1:2.8) than among the settler (1:4.1) and the Innu (1:18.5). The overall crude prevalence rates were about the same for the two sexes; however, of the 69 people positive for HBsAg 42 were male and 27 female.

There was no clear association of HBV seropositivity with relative latitude among the ethnic groups: the crude prevalence rates at the higher v. the lower latitude were 25.7% v. 29.5% for the Inuit, 5.4% and 10.7% v. 1.9% for the settler and 12.7% v. 6.3% for the Innu. For the minor ethnic groups the rates were 17.1% v. 18.8% for the settler in the predominantly Inuit communities and 36.1% and 0% v. 5.4% for the Inuit in the predominantly settler communities; there were too few people in the white and mixed groups in the communities for further analysis.

The age-specific prevalence rates of HBV seropositivity increased with age in all the communities and ethnic groups. The rate was relatively low (4%) for those under the age of 20 years and reached a peak among those aged 45 to 54 years (85% for Inuit, 40% for settler and 37% for Innu) (Fig. 2).

The age-standardized prevalence rates of HBV seropositivity are given in Table III. The rates for the ethnic groups depended on the predominant ethnicity in a community: the rate was higher for the Inuit in the Inuit communities than for the Inuit in the settler communities (27.9% v. 11.3%)

($p < 0.05$). Similarly, the rate was higher for the settler in the Inuit communities than for the settler in the settler communities (18.0% v. 5.9%) ($p < 0.05$). The prevalence rate of HBV seropositivity was higher for the Inuit than for the settler in their respective communities (27.9% v. 5.9%) ($p < 0.05$). For the remaining ethnic groups (Innu, white and mixed) the rate ranged from 0.4% to 9.7%, with essentially no differences.

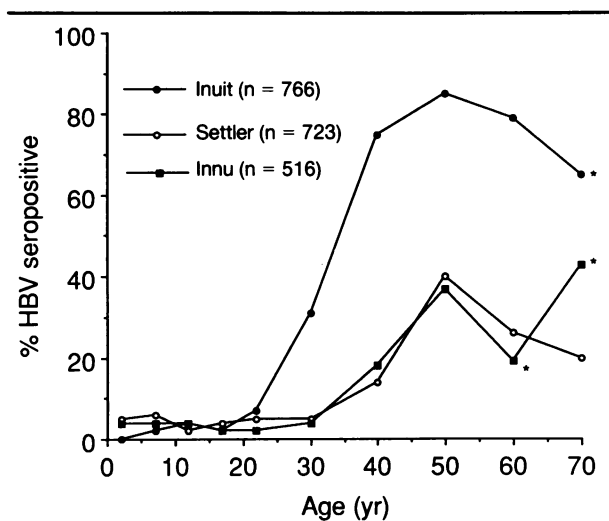


Fig. 2 — Age-specific prevalence rates of hepatitis B seromarkers (antibody to hepatitis B virus [HBV] core antigen [anti-HBc] with antibody to surface antigen [anti-HBs] or with surface antigen [HBsAg] or anti-HBc only) in Inuit, settler and Innu populations. * = fewer than 20 subjects sampled for the age group. Subjects over age 74 years were not included.

Table I — Distribution of study population in seven communities in northern Labrador by community and ethnic group

Community and ethnic group*	1986 population	Ethnic group; no. of subjects						Community participation rate, %
		Inuit	Settler	Innu	White	Mixed	Total	
A (I)	1015	424	164	1	47	0	636	63
B (I)	475	261	69	0	16	0	346	73
C (II)	340	36	202	0	17	0	255	75
D (II)	220	2	121	0	14	0	137	62
E (II)	320	37	160	1	16	0	214	67
F (III)	385	6	7	102	4	7	126	33
G (III)	715	0	0	412	7	23	442	62
Total	3470	766	723	516	121	30	2156	62

*Group I predominantly Inuit, group II settler, group III Innu.

Table II — Crude prevalence rates of hepatitis B virus (HBV) seromarkers by ethnic group

Seromarker	Ethnic group; no. (and %) of subjects					
	Inuit	Settler	Innu	White	Mixed	Total
Antibody to HBV core antigen (anti-HBc) with antibody to surface antigen (anti-HBs) or with surface antigen (HBsAg), or anti-HBc only	202 (26.4)	72 (10.0)	39 (7.6)	3 (2.5)	1 (3.3)	317 (14.7)
HBsAg	53	14	2	0	0	69

Discussion

To keep costs down, our study was designed to assay for HBsAg and anti-HBs only if the initial assay for anti-HBc gave a positive result. This approach would have missed a few subjects with only HBsAg or anti-HBs, but the number is likely to have been small. Also, the overall prevalence of HBV markers is probably not underestimated since anti-HBc is known to persist for life. The overall prevalence rates of HBV markers in our population appear to be within the lower range of previously reported rates for northern populations elsewhere (Table IV). Crude rates are given for our study in Table IV in order to be compatible with the rates from the previously reported studies; the age-standardized rates were not exceedingly different from the crude rates. Our population was more diverse than the native groups previously surveyed, and our results indicated that Labrador Inuit have a slightly higher HBsAg carrier rate than other Inuit populations in northern Canada but not as high as that found in some Inuit villages in Alaska.⁸ The overall prevalence of HBV markers in Labrador Inuit is otherwise comparable to that for other Canadian Inuit populations.^{1,9,10} A previous study of the Newfoundland population (North American whites) indicated the overall crude prevalence rate of HBV markers to be in the range of 3%, a rate consistent with the national average, and even among hospital workers at high risk within the province the rate did not exceed 4.4%.⁵ Thus, the high prevalence of HBV infection in Labrador is in sharp contrast to what had previously been observed for the Newfoundland population.

Our findings show that the prevalence of HBV seromarkers is highest among Inuit in Inuit communities, next highest among settler who live in Inuit communities and among Inuit in settler communities, and lowest among settler in settler communities and among Innu, white and mixed groups. Therefore, ethnic origin is a predominant determining factor of HBV seropositivity. The high prevalence could be attributable to genetic or social predispositions. We did not examine the genetic component, but there was an association of HBV seropositivity with community. This is evidenced by the higher prevalence of seropositivity among settler in Inuit communities than in settler commu-

nities and the lower prevalence among Inuit in settler communities than in Inuit communities. The absence of HBV seropositivity among the 63 whites in the Inuit communities does not detract from the association; the number of whites and the prevalence of seromarkers among them were uniformly low in all the communities. Therefore, it may be concluded that social predisposition appears to be a significant contributing factor to the high prevalence of HBV infection in northern Labrador.

In addition, the general health status of the people in this area is below Canadian standards.¹¹ Alcoholism and sexually transmitted diseases are common; however, there is no illicit parenteral drug use. As for the high prevalence of HBV infection among Inuit and in predominantly Inuit communities, in the 1950s the Inuit in northerly communities were involuntarily resettled to communities A and B (predominantly Inuit) as well as C (predominantly settler). This historic interconnection as well as family ties, the geography and the hunting patterns of northern Labrador traditionally facilitated more travel and a closer link between these three communities than with the other communities. This perhaps explains to some extent the higher prevalence of HBV seromarkers among the Inuit as well as in communities that are predominantly Inuit.

There is considerable evidence that liver damage in HBV infection is immune mediated and that immunocompromised states predispose to the

Table IV — Crude prevalence rates of HBV seromarkers in native populations

Location	% positive	
	For HBsAg	For any seromarker
Alaska ²	6.4	24.2
Alaska ⁸	13.9	54.8
Baffin Zone, NWT ¹	5.1	36.0
Chesterfield Inlet, NWT ⁹	2.3	22.0
Baker Lake, NWT ⁹	4.0	27.0
Arctic Bay, NWT ¹⁰	5.9	25.8
Northern Labrador (present study)		
Inuit	6.9	26.4
Settler	1.9	10.0
Innu	0.4	7.6

Table III — Age-standardized prevalence rates of HBV seromarkers (anti-HBc with anti-HBs or with HBsAg, or anti-HBc only) by ethnic group in respect of the predominant ethnicity of the community

Predominant ethnicity	Ethnic group; rate, %*†				
	Inuit	Settler	Innu	White	Mixed
Inuit	27.9‡	18.0§	0	0.4**	—
Settler	11.3§	5.9 ¶**	0	2.6¶**	—
Innu	16.4	5.6	9.7§ ¶	0	0.6

*For figures in italics the number of subjects was less than 40.

†Rates with a common superscript were not different at $p > 0.05$; Tukey's $w = 8.4$, standard error of the mean = 2.0.

chronic carrier state.¹²⁻¹⁵ Liver disease has been observed to occur only infrequently in the study population, and there has been no reported case of acute hepatitis B in northern Labrador since 1978 (M.B.: unpublished data, 1987). It is also significant that none of the HBsAg carriers detected were positive for HBeAg or anti-HBc IgM. These observations led us to examine the proportion of HBsAg-positive cases to those positive only for anti-HBs or anti-HBc or both. This proportion was found to be higher for the Inuit than for the settler and the Innu. The difference appears to indicate that the Inuit do not clear the antigen or produce antibodies as readily as the other groups. More important, they do not seem to suffer the liver damage that may occur with this process. We speculate that this may be due to a decreased immune response to HBV. Perhaps this is an adaptive mechanism whereby the clinical illness is prevented despite the high prevalence of HBV infection and the chronic carrier state.

The pattern of age-specific prevalence rates of HBV seromarkers found in our population is almost identical to that seen among similar populations in northern Canada (i.e., evidence of HBV infection is uncommon below the age of 20 years, and there is a clear trend of rising prevalence in adulthood).^{1,9} The lack of evidence of HBV infection in children appears to indicate that the disease is transmitted sexually rather than through vertical transmission to the newborn (the Asiatic mode) or early sibling transmission (the African mode). Alternatively, it may indicate a cohort phenomenon, with HBV infection being in retreat, as has been suggested for other Inuit groups.^{16,17} However, this could be established only by resampling the same population several years from now. In the meanwhile, further work is being done to determine whether there is any variation in the prevalence of HBV seromarkers between Inuit who were resettled and those who originated in communities A, B and C. A difference between these groups would support the cohort phenomenon.

Our results clearly show that there are differences in the prevalence of HBV seropositivity between ethnic groups in Labrador. Furthermore, the differences are associated with the mix of ethnic groups. The need for HBV vaccination is least among the white, Innu and mixed groups, higher among settler and highest among Inuit as well as settler in predominantly Inuit communities. Also, the lack of acute cases of hepatitis B and of HBeAg positivity and the indications that the HBV infection is due to horizontal transmission or a cohort phenomenon mean that only household contacts need receive vaccine. Our next strategy is to develop a vaccination program that will direct our efforts and available resources to the groups with the greatest need.

We thank Dr. Mary Watson and all the physicians, nurses, nursing station staff and laboratory personnel of

Grenfell Regional Health Services, St. Anthony and Goose Bay, and the community health representatives of the Labrador Inuit Health Commission for their support, cooperation and assistance. We also thank the personnel of the Provincial Public Health Laboratory, St. John's, for carrying out the serologic testing, and Patricia Kelly, of the Provincial Public Health Laboratory, for secretarial assistance.

References

1. Larke RPB, Froese GJ, Devine RDO et al: Hepatitis B in the Baffin region of northern Canada. In Fortune R (ed): Proceedings of the Sixth International Symposium on Circumpolar Health, Anchorage, Alaska. *Circumpolar Health* 1984; 84: 199-202
2. Schreeder MT, Bender TR, McMahon BJ et al: Prevalence of hepatitis B in selected Alaskan Eskimo villages. *Am J Epidemiol* 1983; 118: 543-549
3. Skinhoj P: Hepatitis and hepatitis B antigen in Greenland. II: Occurrence and interrelation of hepatitis B associated surface, core, and "e" antigen-antibody systems in a highly endemic area. *Am J Epidemiol* 1977; 105: 99-106
4. Heyward WL, Bender TR, McMahon BJ et al: The control of hepatitis B virus infection with vaccine in Yupik Eskimos. *Am J Epidemiol* 1985; 121: 914-923
5. Ratnam S, Tobin AM, Butler RW: Prevalence of markers of hepatitis A and B in Newfoundland and Labrador [abstr]. Presented at the Conjoint Meeting on Infectious Diseases, Vancouver, 1984: 60
6. Steel RGD, Torrie JH: *Principles and Procedures in Statistics*, 2nd ed, McGraw, Montreal, 1980: 633
7. Streiner DL, Norman GR, Blum HM: *P D Q Epidemiology*, B C Decker, Toronto, 1989: 72-74
8. Barrett DH, Burks JM, McMahon B et al: Epidemiology of hepatitis B in two Alaskan communities. *Am J Epidemiol* 1977; 105: 118-122
9. Minuk GY, Postl B, Ling N et al: Hepatitis B viral markers in two epidemiologically distinct Canadian Inuit (Eskimo) settlements. In Fortune R (ed): Proceedings of the Sixth International Symposium on Circumpolar Health, Anchorage, Alaska. *Circumpolar Health* 1984; 84: 203-205
10. Larke RPB, Eaton RDP, Schaefer O: Epidemiology of hepatitis B in the Canadian Arctic. In Harvald B, Hart Hansen JP (eds): *Circumpolar Health 81. Proceedings of 5th International Symposium on Circumpolar Health*, Nordic Council for Arctic Medical Research, Oulu, Finland, 1982: 401-406
11. Wotton KA: Mortality of Labrador Innu and Inuit, 1971-1982. In Fortune R (ed): Proceedings of the Sixth International Symposium on Circumpolar Health, Anchorage, Alaska. *Circumpolar Health* 1984; 84: 139-142
12. Blumberg BS, Gerstley BJS, Hungerford DA et al: A serum antigen (Australia antigen) in Down's syndrome, leukemia, and hepatitis. *Ann Intern Med* 1967; 66: 924-931
13. Sutnick AI, London WT, Gerstley BJS et al: Anicteric hepatitis associated with Australia antigen, occurrence in patients with Down's syndrome. *JAMA* 1968; 205: 670-674
14. Dudley FJ, Scheuer PJ, Sherlock S: Natural history of hepatitis associated antigen positive chronic liver disease. *Lancet* 1972; 2: 1388-1393
15. Wands JR, Davis TE, Humphrey RL et al: Serial studies on hepatitis B surface antigen and antibody following bone marrow transplantation for acute leukemia [abstr]. *Gastroenterology* 1975; 79: 879
16. Minuk GY, Nicolle LE, Postl B et al: Hepatitis virus infection in an isolated Canadian Inuit (Eskimo) population. *J Med Virol* 1982; 10: 255-264
17. Skinhoj P: Persistent virus infections in the Arctic. In Fortune R (ed): Proceedings of the Sixth International Symposium on Circumpolar Health, Anchorage, Alaska. *Circumpolar Health* 1984; 84: 195-198